CLAIMS

1. Use of inhibitors of the expressed proteins, or peptides derived therefrom, of TCF target genes whose expression is regulated by TCF/β-catenin complexes for the preparation of a therapeutical composition for the treatment of cancers in which TCF/β-catenin signalling is deregulated.

2. Use as claimed in claim 1, wherein the inhibitors are antibodies or derivatives thereof directed against the expression products of the target genes that are expressed on the cell membrane.

3. Use as claimed in claim 1 or 2, wherein the antibodies or derivatives thereof are directed against a peptide, which is chosen from the group consisting of: H-YEKELSEYNATALKSPC-NH2; H-PFSPQFASVNC-NH2; H-PGSYKAKQGEGPC-NH2; H-CQMNSVQLDGLPDARY-OH; H-CGYDARQKPEVDQQ-OH; H-CKGVLSNISSITDLGGFD-OH; H-HSALEDVEALHPRKERC-NH2; and H-CNYHSHAGAREHRRGD-OH.

4. Use as claimed in claim 1, 2 or 3, wherein the derivatives are selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, and other antibody-derived molecules.

5. Use as claimed in claim 1, wherein the inhibitors are small molecules interfering with the biological activity of the protein expressed by the target gene.

6. Use of inhibitors of the mRNA transcripts of TCF target genes whose expression is regulated by TCF/β-catenin complexes for the preparation of a therapeutical composition for the treatment of cancers in which TCF/β-catenin signalling is deregulated.

7. Use as claimed in claim 6, wherein the inhibitors are antisense molecules, in particular antisense RNA or antisense oligodeoxynucleotides.

8. Use as claimed in claim 6, wherein the inhibitors are double stranded RNA molecules for RNA interference.

9. Use as claimed in claim 1, wherein the treatment comprises gene therapy.

10. Use as claimed in any one of the claims 1-9, wherein the therapeutical composition is for treatment of Familial Adenomatous Polyposis (FAP).

11. Use as claimed in any one of the claims 1-9, wherein the therapeutical composition is for treatment of colorectal cancer.

12. Use as claimed in any one of the claims 1-9, wherein the therapeutical composition is for treatment of melanomas.

13. Use of TCF target genes whose expression is regulated by TCF/β-catenin complexes for the diagnosis of cancers in which TCF/β-catenin signalling is deregulated.

14. Use as claimed in claim 13, wherein the diagnosis is performed by means of histological analysis of tissue specimens using specific antibodies directed against target gene products, and/or in situ hybridization analysis of TCF/β-catenin target gene expression levels in tissue specimens using specific RNA probes directed against TCF/β-catenin target gene sequences.

15. Use as claimed in any one of the claims 1-14, wherein the target gene is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor

tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

16. Use as claimed in any one of the claims 1-15, wherein the target gene is CD44, comprising a cDNA sequence, which is at least 90% homologous to the cDNA sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18 or Figure 19.

17. Use as claimed in any one of the claims 1-15, wherein the target gene is GPR49, comprising a CDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

18. Use as claimed in any one of the claims 1-15, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21 (SEQ. ID. No 5).

19. Use as claimed in any one of the claims 1-15, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 22 (SEQ. ID. No 7).

20. Use as claimed in any one of the claims 1-15, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in

Figure 23 (SEQ. ID. No 9).

21. Use as claimed in any one of the claims 1-15, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

22. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences as shown in Figure 17 or 18.

23. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

24. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

25. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

26. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

27. Use as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 24 (SEQ ID No. 12).

28. Inhibitor compound directed against the expressed proteins, or peptides derived therefrom, of a TCF target gene the expression of which is regulated by TCF/β-catenin complexes for use in the treatment of colorectal

cancer.

29. Inhibitor compound as claimed in claim 28, which is an antibody or derivatives thereof directed against the expression products of a target gene that is expressed on the cell membrane.

30. Inhibitor compound as claimed in claim 29 wherein the antibodies or derivatives thereof are directed against a peptide, which is chosen from the group consisting of:
H-YEKELSEYNATALKSPC-NH2; H-PFSPQFASVNC-NH2; H-PGSYKAKQGEGPC-NH2; H-CQMNSVQLDGLPDARY-OH; H-CGYDARQKPEVDQQ-OH; H-CKGVLSNISSITDLGGFD-OH; H-HSALEDVEALHPRKERC-NH2; and H-CNYHSHAGAREHRRGD-OH.

31. Inhibitor compound as claimed in claim 29 or 30, wherein the derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, or other antibody-derived molecules.

32. Inhibitor compound as claimed in claim 28, which is a small molecule interfering with the biological activity of the protein expressed by the target gene.

33. Inhibitor compound directed against the transcription product (mRNA) of a TCF target gene the expression of which is regulated by TCF/β-catenin complexes for use in the treatment of colorectal cancer.

34. Inhibitor compound as claimed in claim 33, which is an antisense molecule, in particular an antisense RNA or an antisense oligodeoxynucleotide..

35. Inhibitor compound as claimed in claim 34, which is a double stranded RNA molecule for RNA interference.

36. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is selected from

the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

37. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is CD44, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18, or Figure 19.

38. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is GPR49, comprising a CDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

39. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21(SEQ. ID. No 5).

40. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous

to the sequence shown in Figure 22 (SEQ. ID. No 7).

41. Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 23 (SEQ. ID. No 9).

42. Inhibitor compound Inhibitor compound as claimed in any one of the claims 28-35, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

43. Inhibitor compound as claimed in any of the claims 28-35 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 17 or 18.

44. Inhibitor compound as claimed in any of the claims 28-35 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

45. Inhibitor compound as claimed in any of the claims 28-35 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

46. Inhibitor compound as claimed in any of the claims 28-35 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

47. Inhibitor compound as claimed in any of the claims 28-35 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

48. Inhibitor compound as claimed in any of the claims 1-15 wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein

sequences of Figure 24 (SEQ ID No. 12).

49. Diagnostic agent for diagnosing cancers in which TCF/β-catenin signaling is deregulated.

50. Diagnostic agent as claimed in claim 49, which is a specific antibody directed against the expressed protein of a TCF/β-catenin target gene or an RNA probe specific for a TCF/β-catenin target gene sequence.

51. Therapeutical composition for the treatment of cancers in which the TCF/β-catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more inhibitor compounds as claimed in claims 28-48.

52. Diagnostic composition for the diagnosis of cancers in which the TCF/β-catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more diagnostic compounds as claimed in claim 49 or 50.

53. Compositions as claimed in claim 51 or 52, wherein the cancer is colorectal cancer, melanoma or Familial Adenomatous Polyposis (FAP).

54. Method for the development of therapeutic inhibitor compounds as claimed in claims 28-48, which method comprises the steps:

a) identification of genes regulated by TCF/β-catenin in colon carcinoma cells, in particular by using microarray technologies;

b) validation of one or more of the identified genes as potential target gene(s) for the therapeutic compound by one or more of the following methods:

- confirmation of the identified gene by Northern Blot analysis in colon carcinoma cell-lines;
- determination of the expression profile of

the identified gene in human colorectal tumors and normal tissue;
- determination of the functional importance of the identified target genes for colorectal cancer;

c) production of the expression product of the target gene; and

d) use of the expression product of the target gene for the production or design of a therapeutic compound.

55. Method as claimed in claim 54, wherein the target gene identified in step a) is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.